

In the Claims ✓ ✓ ✓ ✓ ✓

Please cancel Claims 19, 20, 27, 28, 30 and 31 (without prejudice); enter the indicated amendments to Claims 1 to 4, 6, 8 to 18, 21 to 24, 26 and 29; and enter new Claims 32 to 35. Directions for amendment of claims are indicated on the copy of the attached hand amended ("marked up") original claims, showing in manuscript the amendments that have been made and the origins of the new claims. Clean forms of new and rewritten claims are included in the attached "Clean Set of Claims" document.

Remarks

This application seeks protection for certain novel compounds that are inhibitors of the serine protease, Factor Xa, and are useful for the treatment of thrombotic disorders, and for a method of use of these and known compounds for the treatment of thrombotic disorders. It is the national stage of an international application, the claims of which were drafted in accordance with international practice.

Applicants now wish to amend the application to bring it into conformity with United States patent practice, and also to distinguish the claims from the disclosure of WO 99/25686, cited in the International Search Report.

For the assistance of the Examiner, a copy of the original claims is attached, as noted above, showing in manuscript the amendments that have been made.

Claims 19, 20, 27, 28, 30 and 31 have been cancelled, without prejudice.

Claim 1 has been amended to exclude the compound 4-[(3-ethoxybenzoyl-D,L-phenylglyciny]aminomethyl]-1-[4-chlorobenzyl]piperidine. This compound is disclosed as

Compound 2099 in WO 99/25686. The compounds of WO 99/25686 are disclosed as inhibitors of the action of chemokines such as MIP-1 α and MCP-1 on target cells.

Claim 25 has been amended to make it clear that the use of the compound 4-[(3-ethoxybenzoyl-D,L-phenylglyciny)-aminomethyl]-1-[4-chlorobenzyl]piperidine to combat a thrombotic disorder still remains within the scope following the amendment of Claim 1.

Claims 2 to 4, 6, 8 to 15, 17 to 18, 21 to 24, 26 and 29 have been rewritten in single dependent form.

Claim 16 has been made dependent upon any one of claims 1 to 15, 17 to 18 and 21 to 24. Claim 25 now depends from Claim 16.

New claim 32 is based upon a combination of original claims 1, 13, 15, 16, 25, 23, and 6. It is noted that all of the original claims were drafted in multiple dependent form, and hence new claim 32 is fully based on these original claims.

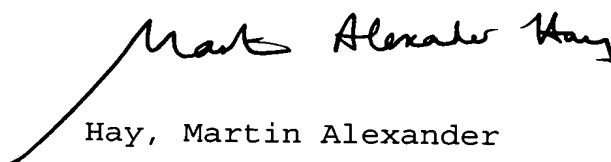
New claim 33 is based upon new claim 32, and additionally incorporates the subject matter of Claims 14, 24 and 5.

New claim 34 is based upon claims 2, 15, 16, 25, 18 22 and 7, and additionally incorporates the preferred definition of R₂ at page 31, line 21 to page 33, line 2. It is noted that the preferences in parentheses have been deleted before moving the text from the description into the claim.

New claim 34 is based upon new claim 34 and claim 9.

Favorable consideration of the application is requested.

Respectfully submitted,



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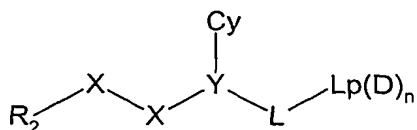
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February 1, 2002

Attachments: Abstract on separate sheet
Hand-amended (marked-up) Claims
Clean Pending Claims

1. ^(amended) A serine protease inhibitor of formula (I):



(I)

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10 optionally being substituted in the 3 and/or 4 position (in relation to the point of attachment of X-X) by halo, nitro, thiol, haloalkoxy, hydrazido, alkylhydrazido, amino, cyano, haloalkyl, alkylthio, alkenyl, alkynyl, acylamino, tri or difluoromethoxy, carboxy, acyloxy, MeSO₂- or R₁, or the
15 substituents at the 3 or 4 positions taken together form a fused ring which is a 5 or 6 membered carbocyclic or heterocyclic ring optionally substituted by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R_{1j}, and optionally substituted in the position
20 alpha to the X-X group (i.e. 6 position for a six membered aromatic ring etc) by amino, hydroxy, halo, alkyl, carboxy, alkoxy, carbonyl, cyano, amido, aminoalkyl, alkoxy or alkylthio with the proviso that R₂ cannot be aminoisquinolyl;

each X independently is a C, N, O or S atom or a CO,
25 CR_{1a}, C(R_{1a})₂ or NR_{1a} group, at least one X being C, CO, CR_{1a}
or C(R_{1a})₂;

each R_{1a} independently represents hydrogen or hydroxyl, alkoxy, alkyl, aminoalkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, alkylaminocarbonyl, alkoxycarbonylamino, acyloxymethoxycarbonyl or alkylamino optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl;

R_1 is as defined for R_{1a} , provided that R_1 is not

unsubstituted aminoalkyl;

Y (the α -atom) is a nitrogen atom or a CR_{1b} group;

Cy is a saturated or unsaturated, mono or poly cyclic, homo or heterocyclic group, optionally substituted by groups

5 R_{3a} or R_{3i}X_i;

each R_{3a} independently is R_{1c}, amino, halo, cyano, nitro, thiol, alkylthio, alkylsulphonyl, alkylsulphenyl, triazolyl, imidazolyl, tetrazolyl, hydrazido, alkylimidazolyl, thiazolyl, alkylthiazolyl, alkyloxazolyl, oxazolyl, alkylsulphonamido,

10 alkylaminosulphonyl, aminosulphonyl, haloalkoxy, haloalkyl, a group of the formula -C(X³)N(R¹¹)R¹² (wherein X³ is O or S; and R¹¹ and R¹² are independently selected from hydrogen, methyl or ethyl or together with the nitrogen atom to which they are attached form a pyrrolidin-1-yl, piperidin-1-yl or
15 morpholino group), or -OCH₂O- which is bonded to two adjacent ring atoms in Cy;

X_i is a bond, O, NH or CH₂;

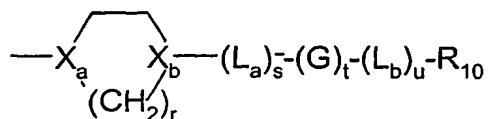
R_{3i} is phenyl, pyridyl or pyrimidinyl optionally substituted by R_{3a}; and

20 R_{1b}, R_{1c} and R_{1j} are as defined for R_{1a};

L is an organic linker group containing 1 to 5 backbone atoms selected from C, N, O and S, or a branched alkyl or cyclic group; and

Lp(D)_n is of the formula:

25



in which:

r is 1 or 2;

X_a is CH and X_b is N;

30 s, t and u are each 0 or 1;

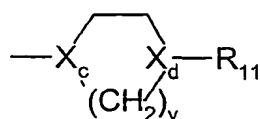
L_a and L_b are each independently selected from a single bond, C=O, O and NR_{1e}, in which R_{1e} is hydrogen or (1-

6C)alkyl;

G is (1-6C)alkanediyl; and

R₁₀ is (1-6C)alkyl; (3-6C)cycloalkyl [which is unsubstituted or substituted by (1-6C)alkyl]; indanyl;

5 pyridyl; tetrahydropyranyl; tetrahydrothiopyranyl; phenyl
 {which is unsubstituted or substituted by one or two R₃ groups
 [wherein R₃ is hydrogen, hydroxyl, alkoxy, alkyl (optionally
 substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or
 cycloalkyl), hydroxyalkyl (optionally substituted by hydroxy,
 10 alkylamino, alkoxy, oxo, aryl or cycloalkyl), alkoxyalkyl,
 alkoxycarbonyl, alkylaminocarbonyl, alkoxycarbonylamino,
 acyloxymethoxycarbonyl, aminoalkyl (optionally substituted by
 hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl),
 alkylamino (optionally substituted by hydroxy, alkylamino,
 15 alkoxy, oxo, aryl or cycloalkyl), amino, halo, cyano, nitro,
 thiol, alkylthio, alkylsulphonyl, alkylsulphenyl, triazolyl,
 imidazolyl, tetrazolyl, hydrazido, alkyl imidazolyl,
 thiazolyl, alkyl thiazolyl, alkyl oxazolyl, oxazolyl,
 alkylsulphonamido, alkylaminosulphonyl, aminosulphonyl,
 20 haloalkoxy, or haloalkyl]}, pyrrolinyl; or a group of formula:



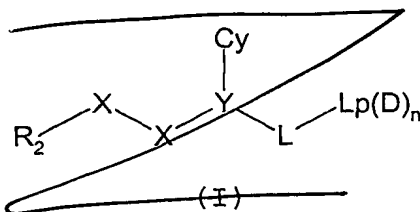
in which v is 1, 2 or 3; one of X_c and X_d is N and the other is
 CH or N (provided that when v is 1, X_c and X_d are not both N);
 25 and R₁₁ is hydrogen, (1-6C)alkyl or when X_d is CH, hydroxy(1-
 6C)alkyl; provided that when t is 0, the sum of s and u is 1;
 when X_b is N, L_a is a bond or C=O; when X_c is N, L_b is a bond
 or C=O; when X_b and X_c are both N, t is 1; and when (L_a)_s-
 (G)_t-(L_b)_u represents an alkyl group and X_b and X_c both
 30 represent N, the alkyl group contains at least two chain
 carbon atoms;

or R₁₀ is hydrogen and s, t and u are each 0;

or the compound of formula (I) that is 4-{[4-methoxybenzoyl-D,L-(2-trifluoromethylthiophenyl)-glycinyllaminomethyl}-1-isopropylpiperidine; or a physiologically-tolerable salt thereof.

5 (amended)

2. A serine protease inhibitor of formula (I):



10 wherein:

R₂ is a 5 or 6 membered aromatic carbon ring optionally interrupted by a nitrogen, oxygen or sulphur ring atom, optionally being substituted in the 3 and/or 4 position (in relation to the point of attachment of X-X) by halo, nitro, thiol, haloalkoxy, hydrazido, alkylhydrazido, amino, cyano, haloalkyl, alkylthio, alkenyl, alkynyl, acylamino, tri or difluoromethoxy, carboxy, acyloxy, MeSO₂- or R₁, or the substituents at the 3 or 4 positions taken together form a fused ring which is a 5 or 6 membered carbocyclic or heterocyclic ring optionally substituted by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R_{1j}, and optionally substituted in the position alpha to the X-X group (i.e. 6 position for a six membered aromatic ring etc) by amino, hydroxy, halo, alkyl, carboxy, alkoxy, carbonyl, cyano, amido, aminoalkyl, alkoxy or alkylthio with the proviso that R₂ cannot be aminoisquinolyl;

each X independently is a C, N, O or S atom or a CO, CR_{1a}, C(R_{1a})₂ or NR_{1a} group, at least one X being C, CO, CR_{1a} or C(R_{1a})₂;

30 each R_{1a} independently represents hydrogen or hydroxyl,
alkoxy, alkyl, aminoalkyl, hydroxyalkyl, alkoxyalkyl,
alkoxycarbonyl, alkylaminocarbonyl, alkoxycarbonylamino,

acyloxymethoxycarbonyl or alkylamino optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl;

R_1 is as defined for R_{1a} , provided that R_1 is not unsubstituted aminoalkyl;

5 Y (the α -atom) is a nitrogen atom or a CR_{1b} group;

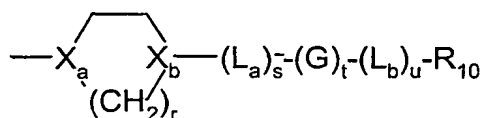
Cy is a saturated or unsaturated, mono or poly cyclic, homo or heterocyclic group optionally substituted by groups R_{3a} or phenyl optionally substituted by R_{3a} ;

each R_{3a} independently is R_{1c} , amino, halo, cyano, nitro,
10 thiol, alkylthio, alkylsulphonyl, alkylsulphenyl, triazolyl, imidazolyl, tetrazolyl, hydrazido, alkyl imidazolyl, thiazolyl, alkyl thiazolyl, alkyl oxazolyl, oxazolyl, alkylsulphonamido, alkylaminosulphonyl, aminosulphonyl, haloalkoxy or haloalkyl; and

15 R_{1b} , R_{1c} and R_{1j} are as defined for R_{1a} ;

L is an organic linker group containing 1 to 5 backbone atoms selected from C, N, O and S, or a branched alkyl or cyclic group; and

$Lp(D)_n$ is of the formula:



in which:

r is 1 or 2;

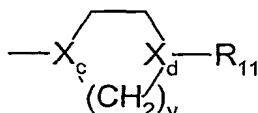
X_a is CH and X_b is N;

s , t and u are each 0 or 1;

25 L_a and L_b are each independently selected from a single bond, C=O, O and NR_{1e} , in which R_{1e} is hydrogen or (1-6C)alkyl;

G is (1-6C)alkanediyl; and

R₁₀ is (1-6C)alkyl; (3-6C)cycloalkyl [which is unsubstituted or substituted by (1-6C)alkyl]; indanyl; pyridyl; tetrahydropyranyl; tetrahydrothiopyranyl; phenyl {which is unsubstituted or substituted by one or two R₃ groups
 5 [wherein R₃ is hydrogen, hydroxyl, alkoxy, alkyl (optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl), hydroxyalkyl (optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl), alkoxyalkyl, alkoxycarbonyl, alkylaminocarbonyl, alkoxycarbonylamino,
 10 acyloxymethoxycarbonyl, aminoalkyl (optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl), alkylamino (optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl), amino, halo, cyano, nitro, thiol, alkylthio, alkylsulphonyl, alkylsulphenyl, triazolyl,
 15 imidazolyl, tetrazolyl, hydrazido, alkyl imidazolyl, thiazolyl, alkyl thiazolyl, alkyl oxazolyl, oxazolyl, alkylsulphonamido, alkylaminosulphonyl, aminosulphonyl, haloalkoxy or haloalkyl}}, pyrrolinyl; or a group of formula:



20 in which v is 1, 2 or 3; one of X_c and X_d is N and the other is CH or N, provided that when v is 1, X_c and X_d are not both N; and R₁₁ is hydrogen, (1-6C)alkyl or when X_d is CH, hydroxy(1-6C)alkyl; provided that when t is 0, the sum of s and u is 1; when X_b is N, L_a is a bond or C=O; when X_c is N,
 25 L_b is a bond or C=O; when X_b and X_c are both N, t is 1; and when (L_a)_s-(G)_t-(L_b)_u represents an alkyl group and X_b and X_c both represent N, the alkyl group contains at least two chain carbon atoms,

or a physiologically-tolerable salt thereof.

(amended)

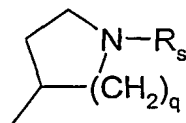
30 3. A serine protease inhibitor according to claim 1 ~~or claim~~

4, wherein R^3 is selected from hydrogen, hydroxyl, methoxy, ethoxy, methyl, ethyl, propyl, 2-propyl, butyl, 2-butyl, t-butyl, pentyl, 2-pentyl, 3-pentyl, isopropylaminomethyl, dimethylamino-methyl, diethylaminomethyl, dimethylaminoethyl, acetyl, hydroxymethyl, hydroxyethyl, carboxy, carboxy(1-5C)alkyl, methoxymethyl, methoxycarbonyl, ethoxycarbonyl, methylaminocarbonyl, dimethylaminocarbonyl, aminomethyl, aminocarbonyl, aminocarbonyl(1-5C)alkyl, methylamino, dimethylamino, ethylamino, formylamino, acetylamino, amino, fluoro, chloro, cyano, nitro, thiol, methylthio, methylsulphonyl, ethylsulphonyl, isopropylsulphonyl, methylsulphenyl, 1,2,4-triazol-2-yl, 1,2,4-triazol-4-yl, 1,2,3-triazol-4-yl, 1,3-imidazol-1-yl, 1,3-imidazol-4-yl, tetrazol-1-yl, tetrazol-5-yl, methylsulphonamido, ethylsulphonamido, propylsulphonamido, methylaminosulphonyl, ethylaminosulphonyl, propylaminosulphonyl, aminosulphonyl, trifluoromethoxy, trifluoromethyl and trichloromethyl.

(amended)

4. A compound according to ~~any of claims 1 to 3~~ wherein r is

5. A compound according to claim 1 wherein $Lp(D)_n$ is of the formula:



25 wherein:

q is 1 or 2;

R_s is hydrogen, $-(CH_2)_c-R_c$, $-CHReR_f$, or $-CH_2-CHReR_f$ [c is 0, 1 or 2; wherein R_c is pyridyl or phenyl (which phenyl may bear a fluoro, chloro, methyl, $CONH_2$, SO_2NH_2 ,

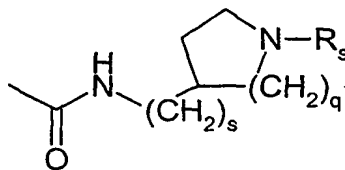
methylaminosulphonyl, dimethylaminosulphonyl,
 methylsulphonylamino, methoxy or methylsulphonyl substituent)
 and R_e and R_f are independently hydrogen or C_{1-3} alkyl; or
 CHR_eR_f is (3-6C)cycloalkyl (which may bear a methyl, ethyl or
 5 hydroxymethyl substituent at the 3- or 4-position, provided
 the substituent is not bonded to the CH group which is bonded
 to L), tetrahydropyranyl, tetrahydrothiopyranyl, pyrrolidinyl
 (which may bear a 1-methyl substituent), piperidinyl (which
 may bear a 1-methyl substituent) (provided that the
 10 tetrahydropyranyl, tetrahydrothiopyranyl, pyrrolidinyl and
 piperidinyl rings are not linked to the piperidin-1,4-diyl
 group through a ring nitrogen atom or a ring carbon atom
 adjacent to a ring oxygen, sulfur or nitrogen atom) or indan-
 2-yl].

15

(amended)

6. / A compound according to ~~any one of claims 1 to 5~~ wherein
 L is CONH, CH_2NHCO , $CONHCH_2$, $CONHCH_2CH_2$ or $CON(Me)CH_2$.

7. A serine protease inhibitor according to claim 2 wherein
 $-L-Lp(D)_n$ is of the formula:



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wherein

q is 1 or 2;

s is 0 or 1; and

R_s is $-(CH_2)_c-R_c$, $-CHR_eR_f$, or $-CH_2-CHR_eR_f$ [wherein c is 1
 25 or 2; R_c is pyridyl or phenyl (which phenyl may bear a fluoro,
 chloro, methyl, $CONH_2$, SO_2NH_2 , methylaminosulphonyl,
 dimethylaminosulphonyl, methylsulphonylamino, methoxy or
 methylsulphonyl substituent) and R_e and R_f are independently

hydrogen or C_{1-3} alkyl; or $CHReR_f$ is cyclopentyl (which may bear a methyl, ethyl or hydroxymethyl substituent at the 3- or 4-position), cyclohexyl (which may bear a methyl, ethyl or hydroxymethyl substituent at the 3- or 4-position),

- 5 tetrahydropyran-4-yl, tetrahydrothiopyran-4-yl, pyrrolidin-3-yl (which may bear a 1-methyl substituent), piperidin-4-yl (which may bear a 1-methyl substituent), or indan-2-yl].

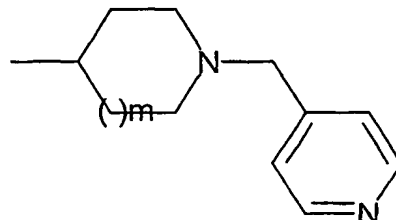
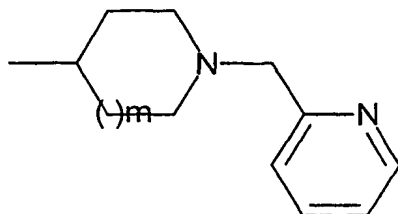
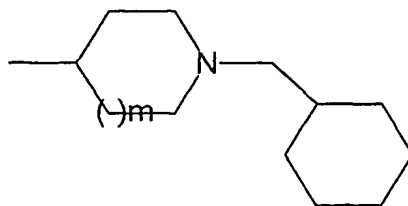
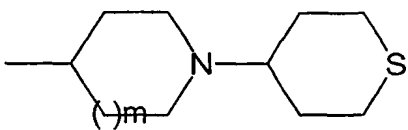
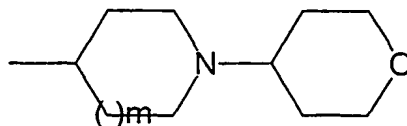
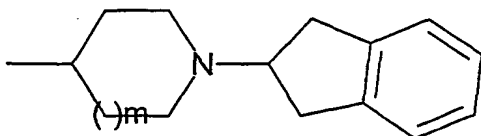
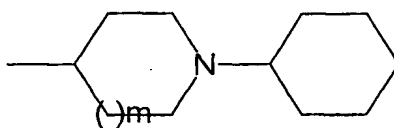
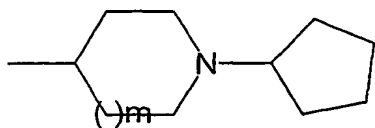
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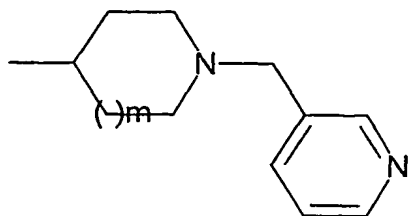
8. A compound according to ~~any of claims 5 to 7~~ wherein q is

10 2.

(amended)

9. A compound according to claim 1 ~~or claim 2~~ wherein $Lp(D)_n$ is selected from one of the following formulae:





wherein m represents 0 or 1.

(amended)

10. A compound according to any of claims ~~15 to~~ 7 wherein R_8 is selected from: hydrogen, methyl, ethyl, prop-2-yl, but-2-yl, pent-3-yl, hept-4-yl, cyclopentyl, cyclohexyl, cyclohexylmethyl, 1-methylpiperidin-4-yl, tetrahydropyran-4-yl, tetrahydrothiopyran-4-yl, phenyl, benzyl, pyrid-2-yl, pyrid-3-yl, pyrid-4-yl, pyrid-3-ylmethyl, pyrid-4-ylmethyl and indan-2-yl.

(amended)

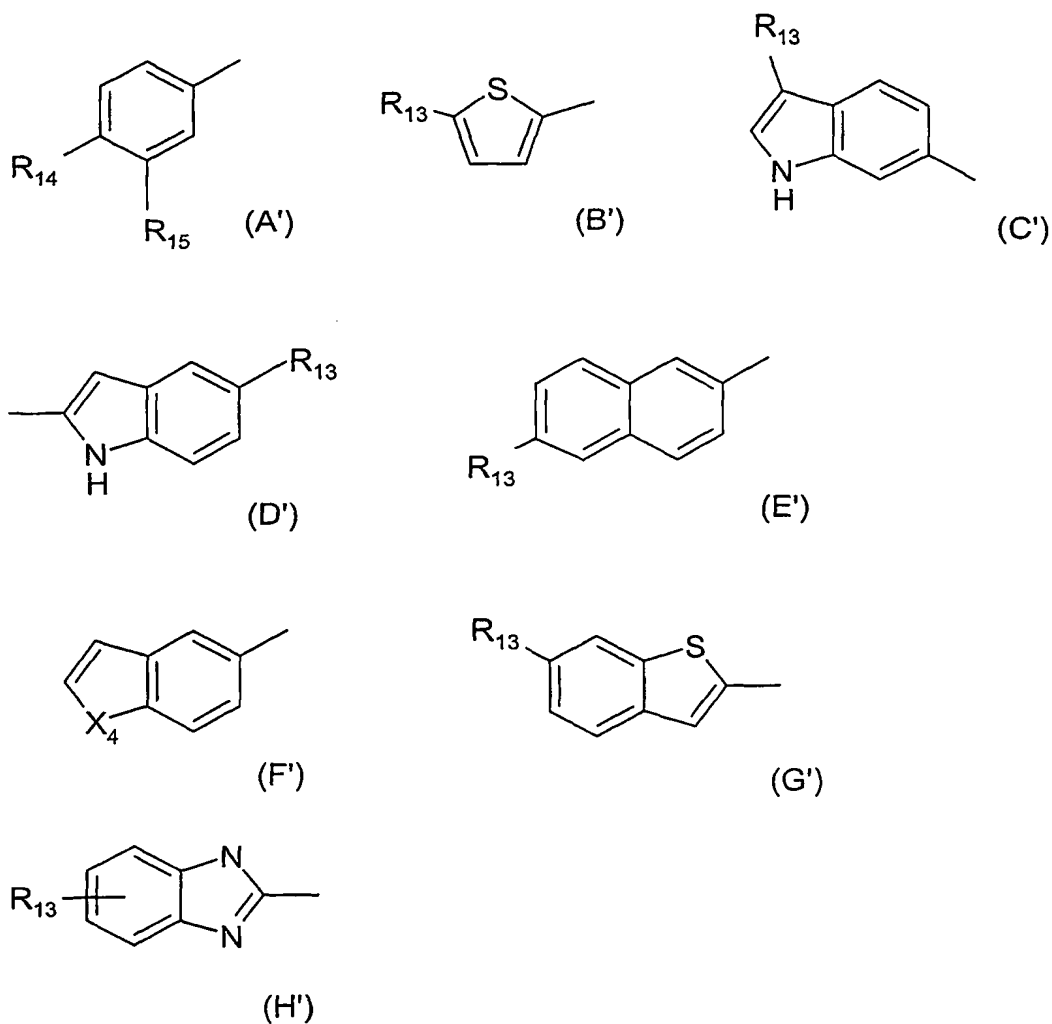
11. A compound according to ~~any one of claims 1 to 10~~ wherein R_2 is phenyl, thien-2-yl, naphthyl, indol-2-yl, indol-6-yl, benzo[b]furan-5-yl, benzo[b]thiophen-2-yl or benzimidazol-2-yl (each of which is optionally substituted as defined in claim 1).

(amended)

12. A compound according to ~~any one of claims 1 to 11~~ wherein optional substituents for R_2 are selected from: fluoro, chloro, bromo, iodo, nitro, thiol, difluoromethoxy, trifluoromethoxy, hydrazido, methylhydrazido, amino, cyano, trifluoromethyl, methylthio, vinyl, ethynyl, acetylamino, carboxy, acetoxy, hydroxy, methyl, ethyl, amido (CONH_2), aminomethyl, methoxy and ethoxy.

(amended)

13. A compound according to ~~any one of claims 1 to 12~~ wherein R_2 is selected from one of the formula (A') to (H'):



wherein X_4 is O or S, R_{13} is selected from hydrogen, fluoro, chloro or methyl and R_{14} is selected from hydrogen, methyl, ethyl, fluoro, chloro, and methoxy and R_{15} is selected from hydrogen, methyl, fluoro, chloro and amino.

(amended)

14. A compound according to claims 1 to 13, wherein R_2 is 4-methoxyphenyl, 3-amino-4-chlorophenyl, indol-2-yl, 5-chloroindol-2-yl, indol-6-yl, 3-chloroindol-6-yl or 3-methylindol-6-yl.

(amended)

15. A compound according to any one of claims 1 to 14 wherein -X-X- is -CONH-.

, 17 to 18 and 21 to 24

(amended)

16. A compound according to any one of claims 1 to 15 wherein Y is CH.

(amended)

17. A compound according to ~~any one of claims 1 to 16~~ wherein Cy is an optionally R_{3a} substituted: phenyl, pyridyl, thienyl, thiazolyl, naphthyl, piperidinyl, furanyl, pyrrolyl, isoxazolyl, isothiazolyl, pyrazolyl, oxazolyl, imidazolyl, 1,2,4-thiadiazolyl, 1,3,4-thiadiazolyl, pyrimidinyl, pridazinyl, quinolyl, isoquinolyl, benzofuryl, benzothienyl or cycloalkyl group, or a phenyl group substituted by R_{3i}X_i in which X_i is a bond, O, NH or CH₂ and R_{3i} is phenyl, pyridyl or pyrimidinyl optionally substituted by R_{3a}.

(amended)

18. A compound according to ~~any one of claims 1 to 17~~ wherein Cy is an optionally R_{3a} substituted: phenyl, pyridyl, thienyl, thiazolyl, naphthyl, piperidinyl or cycloalkyl group.

(cancelled on national phase entry)

19. ~~A compound according to any one of claims 1 to 18 wherein~~
 R_{3a} is selected from hydrogen, hydroxyl, alkoxy, alkyl (optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl), aminoalkyl (optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl), hydroxyalkyl (optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl), alkoxyalkyl, alkoxycarbonyl, alkylaminocarbonyl, alkoxycarbonylamino, alkylamino (optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl), for amino, halo, cyano, nitro, thiol, alkylthio, alkylsulphonyl, alkylsulphenyl, alkylsulphonamido, alkylaminosulphonyl, aminosulphonyl, haloalkoxy, haloalkyl, a group of the formula -C(X³)N(R¹¹)R¹² (wherein X³ is O or S; and R¹¹ and R¹² are independently selected from hydrogen, methyl or ethyl or together with the nitrogen atom to which they are attached form a pyrrolidin-1-yl, piperidin-1-yl or

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~~morpholino group) and -OCH₂O- which is bonded to two adjacent ring atoms in Cy.~~

(cancelled on national phase entry)

20. ~~A compound according to any one of claims 1 to 19 wherein~~

- 5 R_{3a} is selected from hydrogen, hydroxyl, alkoxy, alkyl
(optionally substituted by hydroxy, alkylamino, alkoxy, oxo,
aryl or cycloalkyl), hydroxyalkyl (optionally substituted by
hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl),
alkoxyalkyl, alkoxycarbonyl, alkylaminocarbonyl,
10 alkoxycarbonylamino, alkylamino (optionally substituted by
hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl),
aminoalkyl (substituted by hydroxy, alkylamino, alkoxy, oxo,
aryl or cycloalkyl), halo, cyano, nitro, thiol, alkylthio,
alkylsulphonyl, alkylsulphenyl, alkylsulphonamido,
15 ~~alkylaminosulphonyl, aminosulphonyl, haloalkoxy and haloalkyl~~

(amended)

21. ~~A compound according to any one of claims 1 to 19 wherein~~

- R_{3a} is selected from hydrogen, hydroxyl, methoxy, ethoxy,
methyl, ethyl, methylaminomethyl, dimethylaminomethyl,
20 hydroxymethyl, carboxy, methoxymethyl, methoxycarbonyl,
ethoxycarbonyl, methylaminocarbonyl, dimethylamino-carbonyl,
aminomethyl, CONH₂, CH₂CONH₂, acetyl amino,
methoxycarbonylamino, ethoxycarbonylamino, t-
butoxycarbonylamino, amino, fluoro, chloro, bromo, cyano,
25 nitro, thiol, methylthio, methylsulphonyl, ethylsulphonyl,
methylsulphenyl, methylsulphonylamido, ethylsulphonylamido,
methylaminosulphonyl, ethylaminosulphonyl, aminosulphonyl,
trifluoromethoxy, trifluoromethyl, pyrrolidin-1-ylcarbonyl,
piperidin-1-ylcarbonyl, morpholin-1-ylcarbonyl and -OCH₂O-
30 (which is bonded to two adjacent ring atoms in Cy).

(amended)

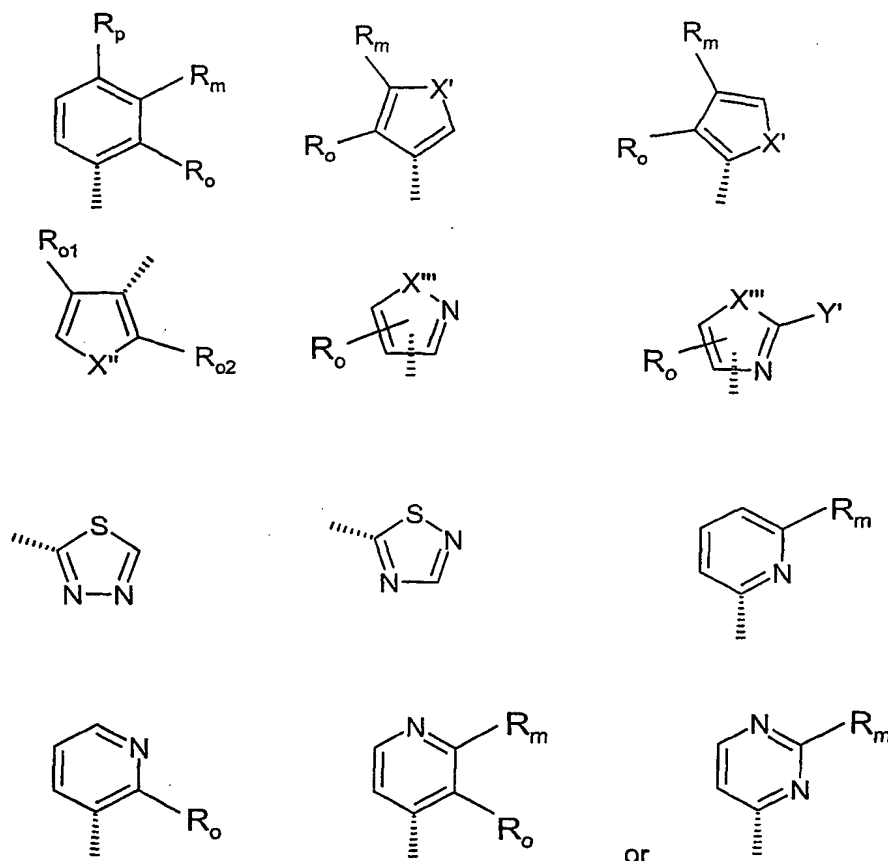
22. ~~A compound according to any one of claims 1 to 19 wherein~~

- R_{3a} is selected from hydrogen, hydroxyl, methoxy, ethoxy,
methyl, ethyl, methylaminomethyl, dimethylaminomethyl,

hydroxymethyl, carboxy, methoxymethyl, methoxycarbonyl, ethoxycarbonyl, methylaminocarbonyl, dimethylamino-carbonyl, aminomethyl, CONH_2 , CH_2CONH_2 , acetyl amino, methoxycarbonylamino, ethoxycarbonylamino, t-
 5 butoxycarbonylamino, amino, fluoro, chloro, cyano, nitro, thiol, methylthio, methylsulphonyl, ethylsulphonyl, methylsulphenyl, methylsulphonylamido, ethylsulphonylamido, methylaminosulphonyl, ethylaminosulphonyl, aminosulphonyl, trifluoromethoxy and trifluoromethyl.

10

(amended)
 23. A compound according to ~~any one of claims 1 to 22~~ wherein Cy is selected from:



15

wherein:

X' is selected from O, S and NMe;

X'' is selected from O and S;

X''' is selected from O, S, NH and NMe;

Y' is selected from hydrogen, amino and methyl;

R_O is selected from hydrogen, methyl, fluoro, chloro, trifluoromethyl, methoxy, methylthio, methylsulphinyl and methylsulphonyl;

R_m is selected from hydrogen, methyl, fluoro, chloro, trifluoromethyl, methoxy, methylthio, methylsulphinyl, methylsulphonyl, carboxy, methoxycarbonyl and a group of the formula -C(X³)N(R¹¹)R¹² (wherein X³ is O or S and R¹¹ and R¹²

10 are independently selected from hydrogen, methyl or ethyl or together with the nitrogen atom to which they are attached form a pyrrolidin-1-yl, piperidin-1-yl or morpholino group);

R_p is selected from hydrogen and fluoro; or

R_O and R_m or R_m and R_p form an -OCH₂O- group; or

15 R_O and R_m together with the ring to which they are attached form a 5 or 6 membered aryl or heteroaryl ring (wherein the heteroaryl ring contains 1 or 2 heteroatoms selected from nitrogen, oxygen and sulfur);

one of R_{O1} and R_{O2} is hydrogen and the other is R_O;

20

(amended)

24. A compound according to ~~any one of claims 1 to 19~~ wherein Cy is selected from phenyl, 2-chlorophenyl, 2-methoxyphenyl, 4-carbamoylphenyl, pyrid-2-yl, pyrid-3-yl, thien-2-yl, thien-3-yl, furan-2-yl, furan-3-yl, imidazol-2-yl, thiazol-2-yl, 25 thiazol-4-yl, thiazol-5-yl, naphthyl, isoquinolin-5-yl, isoquinolin-8-yl, quinolin-4-yl, quinolin-5-yl, and quinolin-8-yl.

(amended)

25. A compound as claimed in ~~any one of Claims 1 to 24~~, in 30 which the alpha atom in Y is carbon and has the conformation that would result from construction from a D-α-aminoacid NH₂-CR_{1b}(Cy)-COOH where the NH₂ represents part of X-X

(amended)

26. A pharmaceutical composition, which comprises a compound

as claimed in ~~any one of claims~~ 1 to 25 together with at least one pharmaceutically acceptable carrier or excipient.

(cancelled on rational phase string)

27. ~~A compound as claimed in any one of claims 1 to 25 for~~
5 ~~use in therapy.~~

(cancelled on national phase entry)

~~28. Use of a compound as claimed in any one of claims 1 to 25 for the manufacture of a medicament for the treatment of a thrombotic disorder.~~

10 (amended)

29. A method of treatment of a human or non-human animal body to combat a thrombotic disorder, which comprises administering to said body an effective amount of a compound as claimed in claim 1, but including the compound 4-(3-ethoxybenzoyl)-5,6-

1. ✓, but including the compound 4 - [(3-ethoxybenzoyl - 1,1-phenyl glycinyl)amino methyl] - 1-[4-chlorobenzyl]piperidine

15 (cancelled or notational phase entry)

~~30. A pharmaceutical composition comprising a compound as claimed in any one of claims 1 to 25 for use to combat a thrombotic disorder;~~

(cancelled on national phase entry)

20 31. ~~A compound of formula I as claimed in claim 1 and named~~
~~in any of the Examples herein, or a physiologically tolerable~~
~~salt thereof.~~

Add new claim 32 to 35

1. The first step is to identify the problem or question that needs to be addressed. This involves understanding the context and the specific requirements of the task.